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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/778,672	02/07/2001	Hsu Ching-Hsaing	12774-002001	4367

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EXAMINER	
LI, QIAN JANICE	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 02/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 09/778,672	**Applicant(s)** CHING-HSAING ET AL.	
	Examiner Q. Janice Li	**Art Unit** 1632	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 22 December 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The reply was filed after the date of filing a Notice of Appeal, but prior to the date of filing an appeal brief. The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: _____.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attachment.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). ____
13. ☐ Other: _____.

Q. Janice Li
Primary Examiner
Art Unit: 1632

Continuation of box 11:

Claims 24-33, 35-39, and 41-49 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Hsu et al (US 5,958,891) and Janeway Jr. (Immunobiology, 1999), in view of Pouwels et al (Intl J Food Microbial 1998;41:155-67) and Medaglini et al (PNAS 1995;92:6868-72, IDS/AI), for reasons of record and following.

Applicants first presented arguments to a previous office action (12/17/03), not the final action, asserting the prokaryotic expression system and eukaryotic expression system are not functionally equivalent in presenting antigen because the former presented the antigen to CD8+ T cells, and the later presented the antigen to CD4+ T cells, and citing '891 patent as supporting evidence.

In response, the Declaration has been addressed previously in the Office action dated 12/17/03, and applicants are reminded that the rejection has been modified since the Declaration was filed. Point 8 of the Declaration asserted that the proteins translated WITHIN the prokaryotic cells are not displayed on MHC I. However, it is noteworthy that Pouwels et al teach when using the lactobacilli for expressing foreign antigens, the production of antigens by the bacteria can occur in three different ways: intracellularly, extracellularly, and surface-bound (§ 7). Apparently, the antigen production by a prokaryotic cell is not limited to translation within said cell, and Medaglini et al have shown that engineered oral commensal bacterium could express a recombinant antigenic protein on its surface, and thus could be effectively used as a vaccine carrier for variety of antigens.
The cited paragraph of the '891 patent in the Remark is under the section of "Background of the invention", and discusses the general knowledge and theory known in the art at the time concerning mechanisms of the immune regulation in allergy, particularly the IgE-mediated allergic response, they are not specific to either the prokaryotic expression system or eukaryotic expression system.

Applicants then argue that they have shown unexpected advantage of the claimed method by a showing that the claimed method achieved more than 80% inhibition of allergen-specific IgE production and did not cause any significant change in antigen-specific IgG production contrary to the Examiner's position.
In response, the Office never intends to speculate the mechanism concerning how the claimed invention functions, this has been set forth previously. The cited Office action dated 12/17/03 or 9/22/04 are responses to applicants' argument that enhancing IgG production teaches away from the suppression of IgE production. The Examiner responded by citing the teaching of Janeway, Jr., and stated the fact that they are not conflicting because Janeway Jr. teaches shifting antibody response from IgE domination to IgG DOMINATION. Indeed, figure 1 of the specification shows an IgG domination in the recombinant bacteria treated group, no matter what the underlying mechanism is.
Concerning the 80% inhibition, it is noted in figure 8 of the '891 patent, the pCMV-Der p5 also causes a more than 80% inhibition of IgE production, thus, the degree of IgE suppression seen in the instant disclosure does not appear to be unexpected.
Further, the court has determined the arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. MPEP 716.01(c).

Applicants then pointed to fig 12.2 of Janeway, asserting the increased production of allergen-specific IgG leads to hypersensitivity and tissue damage, and thus undesired.

In response, it is noted fig 12.2 of Janeway teaches different types of hypersensitivity reaction mediated by different mechanisms. The IgGs shown in the figure differ from the IgG in the instantly disclosed IgE-mediated allergic response in the type of antigen it responds to, the effector mechanism, and the type of consequential clinical hypersensitivity reaction.

Accordingly, for reasons of record and set forth above, the rejection stands.